REMARKS

Claims 1-3, 6-10, 18, 24-26, 30-34, 44, and 46 constitute the pending claims in the present application. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Request for Withdrawal of Finality

Applicants request that finality of the outstanding office action be withdrawn. MPEP 706 states that "the invention as disclosed and claimed should be thoroughly searched in the first action and the references fully applied." Applicants submit that the latest Office Action does not meet this requirement.

As discussed below, the Kosak reference cited by the Examiner under 35 U.S.C. § 102(e) is in fact not prior art against the present application. In particular, the filing date of the cited Kosak patent was later than either of the priority dates of this application. The Examiner inappropriately relied on the date of an earlier-filed application, to which the Kosak patent claimed priority, to establish the pending 102(e) rejection, without consulting the contents of the earlier-filed application. The parent application to the cited Kosak patent is materially different, and entirely lacks the sections of the Kosak patent that were cited and relied on by the Examiner in arguing the prior art rejection. Applicants respectfully submit that for the references to be "fully applied" in accordance with MPEP 706, the Examiner must consider Applicants' arguments herein concerning this priority application. Until the content of the Kosak priority document has been considered by the Examiner as it relates to the pending claims, Applicants submit that the finality of any Office Action in the pending application is premature. Withdrawal of the finality of the pending Office Action is respectfully requested.

Objections to Specification

The Examiner objects to the specification on two grounds. This portion of the Office Action appears to have been copied directly from the previous Office Action without consideration of amendments presented in Applicants' most recent response, mailed May 2, 2002.

First, the Examiner requests that the graphs on pages 53, 57, 58, 59, and 60 be deleted in favor of formal drawings. The Examiner's attention is respectfully drawn to the previous response, filed May 2, 2002, which on page 5 requests deletion of these graphs, and indicates where, in the formal drawings filed with that response, the subject matter is presented. If resolution of this issue requires the further involvement of Applicants, clear and concise instructions as to what further action is needed are respectfully requested.

The Examiner then objects to the use of the term 'Figure' on replacement pages 42, 44, and 48, and to the addition of a "Description of the Figures". Again, Applicants point to the response filed May 2, 2002, which on pages 1-4 provides replacement pages for these pages which do not contain the term 'Figure', and requests the deletion of the "Brief Description of the Figures" section. A new "Brief Description of the Figures" was added in that response, but Applicants submit that this section correctly refers to the formal drawings included with that response. Applicants appreciate the Examiner's suggestions to refer to "Schemes" on these pages, but believe the previously submitted amendments lend more clarity. Reconsideration and withdrawal of this rejection are respectfully requested.

The Claims Comply with 35 U.S.C. § 112, First Paragraph

Claims 1-3, 6-10, 18, 24-27, 30-34, 44, and 46 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which "was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

In particular, the Examiner rejected claims 1-3, 6-10, 18, 24-27, 30-34, 44, and 46, arguing that the terms "comonomer" and "cyclodextrin copolymer" imply a wider scope of subject matter than Applicants have enabled. However, as described in further detail below, in view of the teachings of the application, the extensive knowledge and experience in the art using linker chemistry suitable for generating the claimed copolymers, and the lack of undue experimentation to design, make, test, and use copolymers of the present invention, Applicants contend that the pending claims are fully enabled by the specification.

First, Applicants direct the Examiner's attention to the instant specification, which discloses a wide variety of suitable comonomers, such as on pages 12-15. Page 12, for example, provides substantive guidance on the selection of a suitable comonomer, describing desirable structural and functional attributes for the comonomers. It is clear from the description that the primary function of the comonomer is to link cyclodextrin groups together in a linear chain. Some comonomers contemplated by the invention are acid-labile or biodegradable, and a variety of comonomers with these characteristics are disclosed in the specification. Example 5 on page 31 describes forming a copolymer with DSP, and pages 32-35 describe the preparation of copolymers using DSS, DTBP, cysteamine, and polyethylene glycol. Some of these comonomers, as would be recognized by one of skill in the art, acquire a positive charge under physiological conditions, while others remain neutral. Some of these copolymers are acid-labile, while others are biodegradable. Some of the polymerization reactions place the nucleophile on the cyclodextrin comonomer precursor, while others place the nucleophile on the comonomer A. Pages 37-38 describe the preparation of more complex copolymers in which the linkage between the comonomer and the cyclodextrin monomer is an amidine group, and in one of these, the comonomer includes a labile S-S linkage. Together, these examples show the breadth of enablement and the very disparate linkages and reactions that are enabled by the specification.

But the specification need not be weighed in a vacuum. By the time the instant application was filed, a plethora of suitable linking groups were in wide use in the art, for chemically forming fusion proteins, for dimerizing small molecules or tethering two different molecules together, for attaching molecules to surfaces, and for joining targeting moieties to therapeutic molecules, to name but a few. No challenge would have been presented to one of skill in the art asked to extend the teachings of the present specification to additional linkages and to different cyclodextrin monomer precursors. Indeed, presented herewith as Exhibit **A** is a declaration under 37 C.F.R. §1.132 from Ron Breslow, indicating his expert opinion that the present specification fully enabled one of skill in the art to vary the comonomer widely without resorting to undue experimentation in making or testing the resulting cyclodextrin copolymers.

Finally, Applicants provide herewith as Exhibit **B** papers subsequently published by Applicants that disclose additional reactions, comonomers, and copolymers within the scope of the present disclosure, as further evidence that the teachings of the specification broadly enable the copolymers generically described therein. These papers evidence the investigation of comonomers of varying lengths, and including disparate functional groups, all of which are suitable for purposes described in the present specification. Exhibit **C** is a declaration from inventor Mark E. Davis attesting to the ability of even entry-level chemists to prepare a wide variety of copolymers using routine chemicals and chemical reactions, and includes as Exhibit **D** several manuscripts and other documents that further describe the broad manifestations of the teachings of the present specification. These articles are not offered to render an insufficient disclosure enabling, but rather to demonstrate that the disclosure was in fact enabling when filed. In re Brana, 51 F2d 1560 (CAFC 1995).

The Examiner supports his argument by citing *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 43 U.S.P.Q.2D (BNA) 1398 (Fed. Cir. 1997), for the proposition that "'A definition by function alone does not suffice' to describe a coding sequence 'because it is only an indication of what the gene does, rather than what it is.'" The Examiner is apparently relying on a case centered on the written description requirement to justify an enablement rejection. Applicants respectfully direct the Examiner's attention

to In the matter of the application of Frank S. Barker and Willis G. Pehl, 559 F.2d 588 at 591, 194 U.S.P.Q. (BNA) 470 (C.C.P.A. 1977): "This court has clearly recognized that there is a description of the invention requirement in 35 USC 112, first paragraph, separate and distinct from the enablement requirement. [citations omitted] A specification may contain a disclosure that is sufficient to enable one skilled in the art to make and use the invention and yet fail to comply with the description of the invention requirement." This position is echoed by the MPEP, which clearly acknowledges this distinction at § 2161. Because *Regents of Univ. of Cal. v. Eli Lilly* is concerned with the written description requirement, rather than with enablement, reliance on *Lilly* in the context of an enablement rejection is misplaced.

To the extent the Examiner is attempting to issue a new rejection based on the written description requirement in a final office action, Applicants respectfully assert that the instant claims are adequately supported by the specification. First, the terms to which the Examiner objects have been present since the original filing of this case. The most recent version of the *Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement* appeared in January, 2001, in the Federal Register, Vol. 66, No. 4, pp. 1104-1111 states with respect to original claims drawn to a genus:

> "[t]he written description requirement... may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., **or** by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus....
>
> ... What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." *Guidelines*, page 1106, right column (emphasis added)

As the *2001 Guidelines* suggest, appropriate standard is not whether all the possible variations have been disclosed, but rather whether a sufficient number of

common attributes have been disclosed. Applicants submit that the specification in the pending case not only satisfies the written description requirements as set forth in the *Guidelines*, but, more importantly, also satisfies the guidelines formulated by the Federal Circuit in *Regents of Univ. of Cal. v. Eli Lilly*. In *Lilly* the court stated:

> "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus **or** [by means] of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1569 (emphasis added).

Accordingly, for the description of a genetic invention to be deemed adequate to describe the genus that the claims encompass requires either a recitation of the structure (i.e., sequence) of a representative number of members of the genus **or** a recitation of the common features of the members of the claimed genus. This "recitation of structural features common to the members of the genus" for genetic inventions is analogous to the way in which chemical genera, such as the genera presently claimed, are described, and provides features which readily allow one of skill in the art to recognize the claimed invention. This is in contrast to the way in which the claimed subject matter was recited in Lilly, where nucleic acids were claimed by the name of the cDNA and its origin, without any recitation of sequence or common structural or functional characteristics that could be used by one of skill in the art to readily envision the claimed sequences. Applicants assert that *both* of these prongs, structure and function, are satisfied by the language in the present claims, which describes the common structural features (cyclodextrin monomers and the comonomers that link them together, as well as the linear structure of the polymer as a whole) and the common functional features (such as water solubility), as detailed above. *Lilly* contains even more guidance towards adequately describing the subject matter of such claims, both for chemical materials and genetic materials:

> "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material,

however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." 119 F.3d at 1568

In particular, it is worth noting that the quote on which the Examiner relies is extracted from a sentence clearly directed to "claims to genetic material" instead of from the sentence relating to "chemical materials" that are plainly the subject of the pending claims. If the Examiner continues to rely on this case, Applicants request that the Examiner base the rejection on the portions of that case specifically directed to the subject matter presently being claimed, rather than portions plainly aimed at inventions in a different field of technology. Applicants submit that the pending claims adequately define the claimed subject matter in terms of generic formulae and words associated with well understood structures that indicate with specificity what the generic claims encompass, and accordingly meet the guidelines set forth above and comply with the written description requirement. Reconsideration and withdrawal of this rejection are respectfully requested. If this rejection is to be maintained, a withdrawal of the finality of the Office Action is respectfully requested.

The Claims Comply with 35 U.S.C. § 103(a)

Claims 1-3, 7-10, 18, 24-27, 31-32, 44, and 46 are rejected under 35 U.S.C. §102(e) or alternatively under 35 U.S.C. § 103(a) as being anticipated by Kosak '736. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

As a preliminary matter, Applicants wish to point out that the Examiner's summary of the instant claims is overly narrow. The instant claims cover copolymers of cyclodextrins and α,ω-diamino linkers or *any other suitable linkers for forming linear cyclodextrin copolymers*.

Secondly, as noted above, Applicants respectfully point out that Kosak '736 is prior art against the present application only as of its filing date, December 30, 1998 – after the filing date of the parent to the present application, which fully supports the subject matter now being claimed. Accordingly, Kosak is prior art against the present application only to the extent of the disclosure of its parent application, U.S. Patent Application No. 09/067,921, filed April 29, 1998. Applicants provided the Examiner with a second copy of this application at the interview on January 31, 2003.

Applicants have identified only five pages of this priority document that discuss cyclodextrin polymers. Pages 12, 77, 88, and 102 refer only to cyclodextrin polymers generally, and neither teach nor suggest linear cyclodextrin copolymers having the structural and functional features recited in the present claims. Page 31 provides a synthesis protocol for a cyclodextrin polymer. At the interview on January 31, 2003, the Examiner expressed concern that some amount of linear cyclodextrin copolymer might be formed in this reaction. Applicants first direct the Examiner's attention to the stoichiometry of this reaction – a five-fold excess of BDE to cyclodextrin is used. Thus, as corroborated by the Declaration of Ron Breslow, Exhibit **A**, the likelihood that a substantial number of cyclodextrins will be difunctionalized and capable of forming linear polymers is remote at best. Then, the BDE-modified cyclodextrins are treated with lysine to induce polymerization. Under these uncontrolled conditions, branched polymers will be formed instead of the linear cyclodextrin copolymers presently claimed. Any linear polymers that may form will be present only as trace impurities and will not be amenable to isolation even if they could be detected.

Even if some linear polymers were produced in the reaction described in Kosak's priority document, that fact would be insufficient to anticipate the presently claimed invention. The Supreme Court held, in *Tilghman v. Proctor*, 102 U.S. 707, 711, (1881)

that "If the [claimed invention] were accidentally and unwittingly produced, whilst the operators were in pursuit of other and different results, without exciting attention and without its even being known what was done or how it had been done, it would be absurd to say that this was an anticipation of Tilghman's discovery." Similarly, *International Nickel Co. v. Ford Motor Co.*, 166 F.Supp. 551, 560-61, (S.D.N.Y. 1958) held that "[w]here the allegedly anticipating product was produced merely by chance and never recognized or appreciated, one who later discovers and recognizes the product may patent it." The present situation falls squarely within this analysis. If indeed any linear cyclodextrin polymers were created in the reaction described on page 31, they were created solely by chance, rather than by design. The specification shows absolutely no recognition or appreciation of any linear polymers that may have been so created. Accordingly, to hold the present claims anticipated by Kosak's priority document flies in the face of established precedent of the Supreme Court.

If the Examiner is asserting that the product of Kosak's reaction inherently includes linear polymers, Applicants respectfully direct the Examiner's attention to *In re Robertson*, 169 F3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999), which states that "[t]o establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' ... 'Inherency... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" (quoting *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268-69, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991)) Particularly appropriate to the present situation, *Pfizer, Inc. v. International Rectifier Corp.*, 545 F. Supp. 486, 508, 207 USPQ 397 (C.D. Calif. 1980), *aff'd*, 635 F.2d 357, 217 USPQ 39 (9th Cir. 1982), *cert. denied*, 459 U.S. 1172 (1983) stands for the proposition that "it has never been the law that unrecognized or unappreciated coproduction of a small amount of a compound without a suggestion of that fact being shown in the prior art can be held as anticipating that compound." See also *In re Coordinated Pretrial Proceedings in Antibiotic Actions,* 498 F. Supp. 28, 35 (E.D. Pa. 1980). Thus, it is insufficient as a matter of law for the Examiner to assert that the present claims are

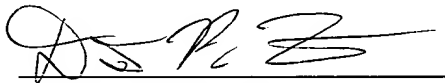
anticipated because of some remote possibility – rather like monkeys typing Shakespeare – that a linear polymer may be formed under the stated conditions.

For all the reasons presented above, Applicants submit that the present claims are novel and non-obvious over Kosak. Reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,



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